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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,703	10/10/2001	Douglas E. Vaughan	1242/39/2	7969
25297	7590	05/27/2004	EXAMINER	
JENKINS & WILSON, PA 3100 TOWER BLVD SUITE 1400 DURHAM, NC 27707			LEITH, PATRICIA A	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 05/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/974,703

**Applicant(s)**

VAUGHAN, DOUGLAS E.

**Examiner**

Patricia Leith

**Art Unit**

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-17 and 37-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-17 and 37-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

Claims 1-4, 6-17 and 37-39 are pending in the application and were examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

#### ***Claim Rejections - 35 USC § 102***

Claims 1, 3, 10 and 12 remain rejected and newly submitted claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al. (1998) or Uehara et al. (1998). Claim 37 specifically recites wherein the risk of cardiovascular disease is reduced (in the body of the claim).

Applicant's arguments were fully considered, but not found persuasive.

Applicant's principal argument resides in the contention that Brown et al. did not teach the administration of an ACE inhibitor to 'healthy' patients. However, the Examiner respectfully disagrees. Applicant states:

'Brown et al. does not teach administering an ACE inhibitor to a healthy subject in order to significantly reduce a risk for cardiovascular disease in the healthy subject. Rather, Brown et al. studied the effect of salt depletion on tPA and PAI-1 activity in the presence or absence of quinapril. Brown et al. did not study reducing the risk of cardiovascular disease in healthy subjects, but instead in subjects having a simulated diseases state (activation of renin-angiotension system) by severely limiting the salt intake (10 mmol/day) of the test subjects" (p.10, Arguments).

However, not all test subjects ingested a salt limited diet, and therefore these subjects did not have an activation of the renin-angiotensin system as clearly shown in Figure 2 A for example. Therefore, these subjects fall within the definition of 'healthy' as defined by Applicant.

Applicant, with regard to the rejection under Uehara et al. argues, "the present claims encompass significantly reducing a risk for cardiovascular disease in healthy subjects. As defined in the specification, "healthy" specifically excludes subjects with diabetes" (p.12, Arguments). However, it cannot be found in the Instant specification where Applicants have defined the term 'healthy' to exclude a patient with diabetes.

Applicant also stresses that the claims specifically state that the treatment is for reducing the risk for cardiovascular disease (as in new claim 37) and that Uehara et al. did not disclose this intended use (p.12, Arguments). However, the Examiner had previously stated that administration of ACE inhibitors by the prior art would have inherently performed the same function as required by the Instant claims because they

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administer the *same compounds* to the *same patients*. Hence, since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims.

### ***Claim Rejections - 35 USC § 103***

Claims 1-17 remain rejected and claims 38-39 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (12/1998) in view of Vaughan (1997). Claim 38 specifically recites wherein the risk of cardiovascular disease is reduced (in the body of the claim) in a post-menopausal patient. Claim 39 is drawn to essentially the same subject matter as claim 16, except claim 39 is dependant upon claim 7.

Applicant's arguments were fully taken into account, but not found convincing.

Applicant argues that neither Brown et al. nor Vaughan teach or suggest the elements of the claimed invention and that Vaughan only suggests ACE inhibitor therapy as having benefit in patients with cardiovascular diseases (p.13, Arguments).

However, it is noted that the prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success.

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*In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the Instant case, although neither reference taught specifically that ACE inhibitors would have been useful for inhibition of cardiovascular diseases in healthy patients, the ordinary artisan would have had a reasonable expectation that it would do so as taught by Brown et al. in view of Vaughan. Again, One of ordinary skill in the art would have been motivated to have administered an ACE inhibitor to a person having a PAI-1 polymorphism, wherein said polymorphism produces excess levels of PAI-1 because PAI-1 is a primary cause of thrombosis ***which can lead to*** cardiovascular disease as taught by Vaughan. It was clear from Vaughan that ACE inhibition subsequently inhibited PAI-1 production.

Thus, although Vaughan did not explicitly teach administration of ACE inhibitors to 'healthy' subjects, the ordinary artisan would have had a reasonable expectation that a person having a polymorph gene which produced excess PAI-1 would have been successfully treated with an ACE inhibitor because ACE inhibition reduced production of endogenously produced PAI-1. It is noted that the term 'healthy' was not defined as a person *not* having a polymorph gene that produces excess PAI-1. On the contrary, the limitation in the claim which further defines 'healthy' states, 'a subject having comprising a PA1-1 polymorphism' which therefore evidences the contention that subjects having comprising a PA1-1 polymorphism fall within the metes and bounds of the term 'healthy'. It is further noted that a person having PAI-1 does not necessarily have any manifestations of a disease state as clearly taught by Vaughan (*supra*).

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Vaughan specifically stated that "These drugs may also protect against thrombosis by reducing the expression of PAI- I normally induced by angiotensin and by augmenting the bradykinin-induced production of t-PA" ('these drugs' referring to ACE inhibitors) (p.15). Thus, Vaughan did clearly provide motivation to administer ACE inhibitors to persons having PA1-1 polymorphism in order to decrease the risk of thrombosis.

It is noted that wherein the newly submitted claims add additional limitations which state that the cardiovascular symptoms are reduced, these are considered intrinsic properties of the method as performed in the prior art and are therefore rejected for the reasoning set forth *supra*.

No Claims are allowed.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith

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Primary Examiner  
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A handwritten signature in black ink, appearing to read "Patricia Leith". The signature is written in a cursive style with a large initial "P" and a horizontal line above the "i" in "Leith".

**PATRICIA LEITH**  
**PRIMARY EXAMINER**